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U.S. Application Serial No. 08/982,272

89. (Amended) A method for expressing a ligand capable of binding to a CD40 ligand receptor in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a [chimeric CD40 ligand] domain or subdomain of human CD40 ligand and a domain or subdomain of non-human CD40 ligand into the cell.

90. (Amended) A method for increasing the concentration of a ligand on the surface of a human cell, wherein the ligand is capable of binding to a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a [chimeric CD40 ligand] domain or sub-domain of human CD40 ligand and a domain or subdomain of non-human CD40 ligand into the human cell, wherein the encoded CD40 ligand has increased stability on the surface of the cell relative to that of a human CD40 ligand.

92. (Amended) The method of claim [91] 89 or claim 90, wherein the non-human CD40 ligand domain or subdomain comprises a murine CD40 ligand domain or subdomain.

99. (Amended) The method of claim [91] 92 wherein the nucleic acid sequence [encoding the chimeric CD40 ligand] comprises SEQ ID NO. 3, SEQ ID NO. 4, SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7 or SEQ ID NO. 20.

100. (Amended) The method of claim 99 wherein the nucleic acid sequence [encoding the chimeric CD40 ligand] comprises SEQ ID NO. 3.

103. (Amended) [The method of claims 89 and 90, wherein the chimeric CD40 ligand comprises] A method for expressing a ligand capable of binding to a CD40 ligand

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receptor in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or subdomain of human CD40 ligand and a domain or subdomain of a non-human ligand selected from the group consisting of CD40 ligand, TNF-alpha, TNF-beta, CD70, CD30 ligand, 4-1 BBL, nerve growth factor and TNF-related apoptosis inducing ligand (TRAIL).

104. (Amended) The method of claim 103 or claim 137, wherein the non-human ligand domain or subdomain comprises a murine ligand domain or subdomain.

108. (Amended) [The method of claims 89 and 90, wherein the chimeric CD40 ligand comprises] A method for expressing a ligand capable of binding to a CD40 ligand receptor in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or subdomain of human CD40 ligand and a domain or subdomain of a human ligand selected from the group consisting of CD40 ligand, TNF-alpha, TNF-beta, CD70, CD30 ligand, 4-1 BBL, nerve growth factor and TNF-related apoptosis inducing ligand (TRAIL).

109. (Amended) The method of claim 108 or 138, wherein the [chimeric] human CD40 ligand comprises Domain IV, or a subdomain of Domain IV, of human CD40 ligand.

Claims 91, 123 - 136 have been cancelled with this Amendment.

Claims 137 - 138 have been added with this Amendment.

Pending Claims Upon Entry of Amendment

87. A method for expressing a CD40 ligand in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a non-human CD40 ligand into the cell.

88. The method of claim 87 wherein the non-human CD40 ligand comprises murine CD40 ligand.

89. (Amended) A method for expressing a ligand capable of binding to a CD40 ligand receptor in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or subdomain of human CD40 ligand and a domain or subdomain of non-human CD40 ligand into the cell.

90. (Amended) A method for increasing the concentration of a ligand on the surface of a human cell, wherein the ligand is capable of binding to a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or subdomain of human CD40 ligand and a domain or subdomain of non-human CD40 ligand into the human cell, wherein the encoded CD40 ligand has increased stability on the surface of the cell relative to that of a human CD40 ligand.

92. (Amended) The method of claim 89 or claim 90, wherein the non-human CD40 ligand domain or subdomain comprises a murine CD40 ligand domain or subdomain.

93. The method of claim 92 wherein the murine CD40 ligand domain or subdomain comprises a murine CD40 ligand extracellular domain.

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94. The method of claim 92 wherein the murine CD40 ligand domain or subdomain comprises Domain III, or a subdomain of Domain III, of the murine CD40 ligand.

95. The method of claim 92 wherein the murine CD40 ligand domain or subdomain comprises Domain IV, or a subdomain of Domain IV, of the murine CD40 ligand.

96. The method of claim 94 wherein the murine CD40 ligand further comprises Domain IV, or a subdomain of Domain IV, of the murine CD40 ligand.

97. The method of claim 92 wherein the murine CD40 ligand comprises Domain I, or a subdomain of Domain I, of the murine CD40 ligand.

98. The method of claim 92 wherein the murine CD40 ligand comprises Domain II, or a subdomain of Domain II, of the murine CD40 ligand.

99. (Amended) The method of claim 92 wherein the nucleic acid sequence comprises SEQ ID NO. 3, SEQ ID NO. 4, SEQ ID NO. 5, SEQ ID NO. 6, SEQ ID NO. 7 or SEQ ID NO. 20.

100. (Amended) The method of claim 99 wherein the nucleic acid sequence comprises SEQ ID NO. 3.

101. The method of claims 89 and 90, wherein the introduction of the nucleic acid sequence into the cell results in induced expression of surface markers on the cell.

102. The method of claim 101, wherein the surface markers comprise CD54, CD80, CD86, CD58, CD70, or CD95.

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103. (Amended) A method for expressing a ligand capable of binding to a CD40 ligand receptor in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or subdomain of human CD40 ligand and a domain or subdomain of a non-human ligand selected from the group consisting of CD40 ligand, TNF-alpha, TNF-beta, CD70, CD30 ligand, 4-1 BBL, nerve growth factor and TNF-related apoptosis inducing ligand (TRAIL).

104. (Amended) The method of claim 103 or claim 137, wherein the non-human ligand domain or subdomain comprises a murine ligand domain or subdomain.

105. The method of claim 104 wherein the murine ligand comprises Domain III, or a subdomain of Domain III, of the murine ligand.

106. The method of claim 104 wherein the murine ligand comprises Domain IV, or a subdomain of Domain IV, of the murine ligand.

107. The method of claim 105 wherein the murine ligand further comprises Domain IV, or a subdomain of Domain IV, of the murine ligand.

108. (Amended) A method for expressing a ligand capable of binding to a CD40 ligand receptor in a human cell that expresses a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or subdomain of human CD40 ligand and a domain or subdomain of a human ligand selected from the group consisting of CD40 ligand, TNF-alpha, TNF-beta, CD70, CD30 ligand, 4-1 BBL, nerve growth factor and TNF-related apoptosis inducing ligand (TRAIL).

109. (Amended) The method of claim 108 or 138, wherein the human CD40 ligand comprises Domain IV, or a subdomain of Domain IV, of human CD40 ligand.

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110. The method of claim 109 wherein the chimeric CD40 ligand comprises Domains I, II, and IV of human CD40 and Domain III of human CD70 receptor ligand.

111. The method of claims 89 and 90, wherein the cell comprises a human neoplastic cell.

112. The method of claims 89 and 90 wherein the cell comprises a cell from connective tissue surrounding neoplastic cells.

113. The method of claim 111, wherein the cell comprises a neoplastic B cell.

114. The method of claim 113, wherein the neoplastic B cell comprises a CLL cell.

115. The method of claim 113 wherein the neoplastic B cell is derived from a patient with a B cell malignancy.

116. The method of claim 111 wherein the neoplastic cell comprises a T cell.

117. The method of claim 111 wherein the neoplastic cell comprises a dendritic cell.

118. The method of claim 111 wherein the neoplastic cell comprises a monocyte.

119. The method of claim 111 wherein the neoplastic cell comprises a myelomonocyte.

120. The method of claim 111 wherein the neoplastic cell comprises a cell derived from a breast tumor.

121. The method of claim 111 wherein the neoplastic cell comprises a cell derived from an ovarian tumor.

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122. The method of claim 111 wherein the neoplastic cell comprises a cell derived from a lung tumor.

137. (New) A method for increasing the concentration of a ligand on the surface of a human cell, wherein the ligand is capable of binding to a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or sub-domain of human CD40 ligand and a non-human ligand selected from the group consisting of CD40 ligand, TNF-alpha, TNF-beta, CD70, CD30 ligand, 4-1 BBL, nerve growth factor and TNF-related apoptosis inducing ligand (TRAIL).

138. (New) A method for increasing the concentration of a ligand on the surface of a human cell, wherein the ligand is capable of binding to a CD40 ligand receptor, comprising introducing a nucleic acid sequence encoding a domain or sub-domain of human CD40 ligand and a human ligand selected from the group consisting of CD40 ligand, TNF-alpha, TNF-beta, CD70, CD30 ligand, 4-1 BBL, nerve growth factor and TNF-related apoptosis inducing ligand (TRAIL).

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Notes/Comments:

Dear Examiner Gambel: Attached are proposed amended claims that seek to overcome some of the issues you raised during our interview of January 22. Pls. review and contact me with any comments that you can provide.

Thanks, Rita Abbati

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